REMARKS

Claims 21-40 were pending.

Claims **24**, **27**, **29**, **34** and **39** have been canceled.

Independent claims **21**, **25** and **35** have been amended to add the phrase "wherein the linker is 5-thio-pentan-1-ol."

Support for the phrase "wherein the linker is 5-thio-pentan-1-ol" appears, e.g., in previously presented claims **24** and **29**.

Claims **33** has been amended to depend on claim **28** due to cancellation of its previous base claim **29**.

No new matter has been added. Applicant respectfully requests that the amendments be entered.

Applicant through her attorney on the record and identified below appreciates Examiner ARNOLD, ERNST V for granting Applicant a telephone interview and helpful suggestions on proposed claim amendments on February 3, 2010.

The following remarks herein are considered to be responsive thereto.

Claim Rejections – 35 USC § 112 First Paragraph

The Examiner has rejected claim **27** under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant respectfully traverses the rejections. To advance the prosecution, however, claim **27** has been canceled, which renders the rejection moot.

It is thus respectfully requested that the rejections be withdrawn.

Claim Rejections – 35 USC § 101

The Examiner has rejected claim **27** and **39** under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter.

Applicant respectfully traverses the rejections. To advance the prosecution, however, claims **27** and **39** have been canceled, which renders the rejection moot.

It is thus respectfully requested that the rejections be withdrawn.

Claim Rejections – 35 U.S.C. §102(b)

The Examiner has rejected claims **21-23**, **35** and **36** under 35 U.S.C. §102(**b**) as being anticipated by de la Fuente et al. (Angew Chem 2001, 113(12), 2317-2321).

Applicant respectfully traverses the rejection. To advance the prosecution, however, Applicant has amended these claims to recite the linker 5-thio-pentan-1-ol.

Legal Standard

MPEP § 2131.01 states that "**[t]o anticipate a claim, the reference must teach every element of the claim**." [emphasis added.]

These claims each require, among other things, "5-thio-pentan-1-ol."

The Examiner has acknowledged that de la Fuente et al. fail to teach 5-thio-pentan-1-ol.

Thus, de la Fuente et al. do not anticipate claims **21-23**, **35** and **36**.

During the 2/03/2010 telephone interview, the Examiner recognized that both references fail to teach the linker 5-thio-pentan-1-ol, and suggested that claims 24 and 21 be merged as he considered that the presence of the linker 5-thio-pentan-1-ol distinguishes the claimed invention from prior art.

Applicant contended that the size and the linker 5-thio-pentan-1-ol are each distinguishable from the cited reference. To advance the prosecution, however, Applicant has amended the independent claims to recite the linker 5-thio-pentan-1-ol.

It is believed that all amended, independent claims are now in the condition for allowance.

Thus, Applicant respectfully requests that the rejections be withdrawn.

Reply to the Examiner's allegations

The Examiner has alleged that De la Fuente et al. disclose a diameter of 1.8 nm which is about 2 nm of instant claim **21**.

The Examiner erred on this point under MPEP §2131.03, III.

MPEP §2131.03, III states that "**prior art which teaches a value or range that is very close to, but does not overlap or touch, the claimed range, does not anticipate the claimed range.**" **[Emphasis added.]**

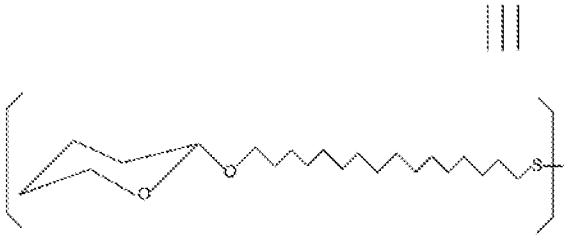
The Examiner has further alleged that De la Fuente et al. disclose scheme 1, in which "a monosaccharide is attached to the nanoparticle thus anticipated instant claims **22** and **35**.

Applicant respectfully submits that the Examiner erred on this point as well.

The entire article of De la Fuente mentioned nothing about a monosaccharide that is conjugated to a gold nanoparticle.

As Applicant pointed out in the 10/13/2009 reply, de la Fuente et al. teach selection of two biologically significant oligosaccharides, the **disaccharide lactose** and the **trisaccharide Le^x**.

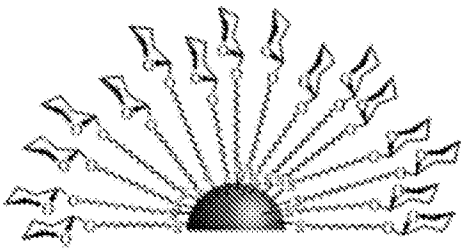
The scheme 1 in de l a Fuente et al. shows the **thio-derivatized disaccharide lactose 1-2** and the **thio-derivatized trisaccharide Le^x 3** have been prepared to functionalize gold nanoparticles. For schematic illustrations, lactose and Le^x each are represented as a thiol-derivatized neoglycoconjugages as shown below:



The symbol "|||" means "are illustrated as below."

Thus, the below symbol represents **thio-derivatized disaccharide lactose 1-2** or the **thio-derivatized trisaccharide Le^x 3, rather than a monosaccharide.**

Accordingly, the drawing shown below is a schematic illustration of lactose or Le^x conjugated gold glyconanoparticle, rather than a monosaccharide conjugated gold nanoparticle.



Further evidence to support Applicant's reasoning is the context and the contents of the article. Nowhere in de la Fuente's article mentioned a word of monosaccharide. It is improper for the Patent Office to read the scheme 1 of de la Fuente as inherently teaching or suggesting a monosaccharide conjugated nanoparticle.

Thus, claims **22** and **35** are not anticipated by de la Fuente.

Moreover, claim **22** depends on claim **21**. The base claim **21** is not anticipated by de la Fuente et al. The dependent claim **22** is thus unanticipated by de la Fuente et al.

Claims **23** and **36** are novel over de la Fuente because they depend on claims **21** and **35**, respectably, and claims **21** and **35** are novel over de la Fuente as discussed above.

It is thus respectfully requested that the 102 rejection be withdrawn.

Claim Rejections – 35 U.S.C. §103

The Examiner has rejected Claims **21-40** under 35 U.S.C. §103(a) as being unpatentable over de la Fuente et al. (Angew Chem 2001, 113(12), 2317-2321 and Penades et al. (WO 2002/032404).

The rejections over Claims **24**, **27, 29**, **34** and **39** are moot due to cancelations of these claims.

Legal Standard for Obviousness Rejection

The legal standard for establishing a prima facie case of obviousness requires that the references "teach or suggest all the claim limitations." *See* MPEP §2143. (Emphasis added.)

Independent claims **21**, **25** and **35** each require, among other things, "5-thio-pentan-1-ol."

The Examiner has acknowledged that de la Fuente et al. fail to teach 5-thio-pentan-1-ol.

The Examiner has alleged it "would have been obvious . . . to use the linker 5-thio-pentan-1-ol, as suggested by Penades et al. in the composition of de la Fuente et al., and produce the instant invention."

However, Penades et al. does not teach or suggest the linker 5-thio-pentan-1-ol.

In fact, **the reference Penades et al. is identical to de la Fuente as to the teaching of the thiol linkers because the two teach exactly the same thing, and even using exactly the same words verbatim.** Penades et al. teach that "[t]he synthesis of the disulfides 1, 2 and 3 was carried out by glycosidation of the conveniently protected lactose and Le^x derivative with 11-thioacetate-3,6, 9- trioxa-

undecanol (for 1) and 11-thioacetate undecanol (for 2 and 3)." See Penades et al. page 26, lines 24-28 and de la Fuente et al. page 2319, lines 2-7 for comparisons: 100% identical.

Two inventors in the reference Penades et al. are the coauthors of the reference de la Fuente.

de la Fuente et al. fail to teach 5-thio-pentan-1-ol, as the Examiner has acknowledged. So do Penades et al.

Thus, **the Examiner is essentially citing de la Fuente twice in making §103 rejections as to the element 5-thio-pentan-1-ol.**

Since the combination of the reference does not teach or suggest all the claimed limitations, the Examiner has failed to make a prima facie case of obviousness.

Because neither de la Fuente nor Penades teach or suggest the linker 5-thio-pentan-1-ol, the combination would not result in the instant invention.

The Examiner also failed to provide a motivation for replacing de la Fuente's linker with 5-thio-pentan-1-ol.

The Examiner has intentionally omitted the fact that neither de la Fuente nor Penades teach or suggest the linker 5-thio-pentan-1-ol. The Examiner made up a far-stretched motivation alleging that "it is then merely judicious selection of the thiol linker in the absence of evidence to the contrary."

Selecting 5-thio-pentan-1-ol could not have been an "obvious to try" because this is not a case where there were a limited number of thio-derivatives to choose from for making the combination.

It is unfair to Applicant that the Examiner in one way has alleged "the linker 5-thio-pentan-1-ol, as suggested by Penades et al. while in fact there was not such teaching or suggestion in Penades, and in another way alleged that "it is merely judicious selection of the thiol linker"

when it is patently obvious to one of ordinary skilled in the art there is an infinite number of thio-derivatives out there.

In this case, neither of the references cited teaches or suggests the linker 5-thio-pentan-1-ol. Thus, even if there were a motivation to combine, the combination would not result in the claimed invention.

Accordingly, the primary reference de la Fuente et al. and the secondary reference Penades et al., either alone or in combination, does not anticipate or render the independent claims **21**, **25** and **35** obvious.

The court has held that if an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Dependent claims **22-23, 26-33**, and **36-38** and **40** are nonobvious because their respective base claims are nonobvious over the combination of the cited references as discussed above.

Moreover, dependent claim **32** further requires Pk antigen, which is not taught or suggested by either de la Fuente or Penades et al.

The Examiner has acknowledged that de la Fuente et al. fails to teach a Pk antigen or a pathogen bound to the nanoparticle.

The Examiner has repeated the same unfair practice: In one way, the Examiner has alleged it "would have been obvious . . . to have a Pk antigen . . ., as suggested by Penades et al., and produce the instant invention," and in another way, the Examiner has alleged that "it is merely selection of the proper antigen such as Pk antigen."

However, <u>Penades et al. do not teach or suggest Pk antigen. It is erroneous to state that the reference teaches or suggests something when in fact it does not</u>.

With regard to the Examiner's allegation of "judicious selection," **again this is not a case where there are a limited number of antigens to choose from for making the combination. It could not have been obvious for one of ordinary skill in art to select Pk antigen to replace de la Fuente's lactose or Le^x antigen because there is an infinite number of antigens out there and the cited reference does not teach or suggest Pk antigen.**

The teaching or suggestion to make the claimed combination must be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

It appears to Applicant that the Examiner has been finding the teaching and suggestion in Applicant's disclosures as to the element Pk antigen and the linker 5-thio-pentan-1-ol, which is impermissible according to patent law.

With regard to the allegation that it "would have been obvious . . . to have a pathogen bound to the nanoparticle . . ., as suggested by Penades et al., and produce the instant invention," the Examiner provides a routine motivation by alleging that "it is merely selection of the proper antigen such as Pk antigen to bind the corresponding pathogen."

As Applicant has pointed out above, Penades et al. do not teach or suggest Pk antigen conjugated nanoparticle, and there are an infinite number of antigens. It would not have been obvious for one of ordinary skill in the art to select Pk antigen to bind a corresponding pathogen.

Moreover, the court has held that if the proposed modification or combination of the prior art would change the principles of operation of the prior art invention being modified, then the teaching of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

To have a Pk antigen to replace the lactose or Lex conjugated to the gold nanoparticle of de la Fuente's and then to bind to a pathogen onto the Pk antigen would frustrate the purpose of de

la Fuente et al. because the 3D model gold glyconanoparticles designed by de la Fuente et al. are to solve the challenges faced in studying "a hemophilic carbohydrate-carbohydrate interaction between the Lewis^x antigen," and "a heterotropoic interaction between glycosphingolipid patches of GM3 and Gg3 involved in metastasis of melanoma cells." *See* page 2318, first paragraph.

Furthermore, Penades et al. do not teach to have a pathogen bound to a Pk antigen. Penades et al. teach that "nanoparticles in which the carbohydrate (saccharide) group is an antigen can be administered as a vaccine." See page 12, lines 14-23.

The claimed invention must be compared as a whole to a prior art reference. Claim limitations are not puzzle pieces to be matched to atomized prior art reference suggestions, and thus examined out of context. As with obviousness in combining prior art references, only if the prior art aligns with the claimed invention in principles of operation may a prior art reference be considered anticipatory.

In 10/13/2009 reply, Applicant has pointed out de la Fuente cannot be reasonably construed as anticipatory because it does not teach or suggest all the claimed inventions. Applicant has also pointed out that the purpose/problem being solved (nature of the problem), and structure of de la Fuente are not aligned with the claimed invention. To refresh the Examiner's memory, Applicant respectfully cites an excerpt of the 10/13/2009 reply as follows:

> "The gold glyconanoparticles of de la Fuente et al. are **structured and operated differently** from the clamed invention. The invention is structured to operate as a tool for labeling cellular proteins that bind specifically to the conjugated saccharides.
>
> The principles of operation in de la Fuente et al. are presentation of a "three-dimensional (3D) model system for the study of carbohydrate interactions." The 3D model gold glyconanoparticles designed by de la Fuente et al. are to solve the challenges faced in studying "a hemophilic carbohydrate-carbohydrate interaction between the Lewis^x antigen," and "a heterotropoic interaction between glycosphingolipid patches of GM3 and Gg3 involved in metastasis of melanoma cells." *See* page 2318, first paragraph.

By the nature of their structural design, the gold glyconanoparticles in de la Fuente et al. each have necessary structural components to result in Lewis^x antigen interactions and/or to allow potential interactions between glycosphingolipid (GSL) microdomains. Fuente's gold glyconanoparticles were intended to mimic glycosphingolipid (GSL) microdomains, the lipid chain is thus necessary. The gold glyconanoparticles therein contain undecanol (11 carbons) as one part of his glyconanoparticle to mimic cell surface lipid bilayer. Their system "consists of gold nanoclusters functionalized with neoglycoconjugates of biologically significant **oligosaccharides**." (page 2318, column 1, first paragraph) Their gold glyconanoparticles comprises either the disaccharide lactose or the trisaccharide Le^x so that the Le^x-Au was able to show self-recognition and self-aggregation so as to mimic the "hemophilic carbohydrate-carbohydrate interaction between the Lewis^x antigen," which "seems to be responsible for morula compaction." (page 2318, first paragraph; and page 2320, first paragraph.)

One of ordinary skill in the art at the time the invention was filed would not have been motivated to modify the oligosaccharides lactose and Le^x of de la Fuente et al. with Applicant's monosaccharides such as mannose, galactose and glucose, and/or Pk antigen because such a modification would not align with the principles of operation in prior art.

Furthermore, one of ordinary skill in the art at the time the invention was filed would not have been motivated to modify the two linkers 11-thioacetate-3, 6, 9-trioxa-undecanol and 11-thioacetate undecanol (11 carbons) of de la Fuente et al. with Applicant's linker 5-thio-pentan-1-ol (5 carbons) because such a modification would deviate from the prior at principles of operation, i.e., to mimic glycosphingolipid (GSL) clustering and study potential interactions between glycosphingolipid (GSL) microdomains. *See* page 2318, first paragraph; page 2319, column 1, last paragraph."

Accordingly, Applicant respectfully requests that the § 103 rejections be withdrawn.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical correction only.

It is thus believed that the application is in condition for allowance at least for the above reasons and such allowance is respectfully requested.

CONCLUSION

Applicant respectfully submits that the foregoing Amendment and Response place this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference to facilitate the prosecution of this application, or that there are any informalities that can be corrected by an Examiner's amendment, please call the undersigned at 650-557-4464.

Respectfully submitted,

February 3, 2010

/Hsiu-Ming Saunders /
Hsiu-Ming Saunders, Ph.D.
Attorney for Applicants on the Record
Reg. No. 47,055

IPC INTELLECTUAL PROPERTY CONNECTIONS, INC.
299 Old County Road, Suite 28
San Carlos, CA 94070
Tel: (650)-557-4464
Mobile: (651) 235-7129
Fax: (650) 472-9153
Customer No. 74603